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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/684,212	10/10/2003	Lin Zhi	45026.00127.UTL1	8674

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EXAMINER

AULAKH, CHARANJIT

ART UNIT PAPER NUMBER

1625

DATE MAILED: 10/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/684,212

Applicant(s)

ZHI ET AL.

Examiner

Charanjit S. Aulakh

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 August 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-25 and 41-55 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-25 and 41-55 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>2 pages</u> . | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

1. According to paper filed on Aug. 17, 2005, the applicants have filed a RCE and furthermore, amended claims 1, 5, 9-11, 15, 19, 23, 24 and added new claims 41-55.
2. The restriction is withdrawn since the method claims 41-55 are directed to using compounds of formulae (I) or (II) of group I.
3. Claims 1-25 and 41-55 are now pending in the application.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-25 and 41-55 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The following eight different factors (see *Ex parte Foreman*, 230 USPQ at 547; *Wands*, In re, 858 F. 2d 731, 8 USPQ 2d 1400, Fed. Cir. 1988) must be considered in order for the specification to be enabling for what is being claimed: Quantity of experimentation necessary, the amount of direction or guidance provided, presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability and the breadth of claims. In the instant case, the specification is not enabling based on at least

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four of the above mentioned eight different factors such as quantity of experimentation necessary, the amount of direction or guidance provided, the state of the prior art, presence of working examples and the breadth of claims.

The instant compounds are agonist at progesterone receptor as shown by data in tables 3 and 4 on pages 76 and 77. Therefore, based on this data, the instant compounds will have utility in treating disease conditions where progesterone receptor agonists are well known in the prior art to have therapeutic effect. There is no teaching either in the specification or prior art references showing therapeutic effect of progesterone receptor agonists. There are no working examples present showing efficacy of instant compounds in known animal models of any disease conditions where progesterone receptor agonist activity is implicated in their etiology. The instant compounds of formulae (I) and (II) encompass hundreds of thousands of compounds based on the values of variables R8 and R9 and therefore, in absence of such teachings, guidance and working examples, it would require undue experimentation to demonstrate the efficacy of instant compounds in known animal models of all disease conditions where progesterone receptor agonist activity is implicated in their etiology.

It is well known in the art that the efficacy of a prodrug following in vivo administration depends upon release of parent compound to its target in vivo. A prodrug of any compound does not necessarily mean that the parent compound will be released in vivo since it is influenced by various factors such as absorption, metabolism, degradation by esterases etc. It is of note that there is not even a single example present in the specification of any prodrug. As stated earlier, the instant compounds of

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formulae (I) and (II) encompass hundreds of thousands of compounds based on the values of variables R8 and R9 and therefore, in absence of such teachings, guidance and working examples, it would require undue experimentation to prepare different prodrugs of all compounds encompassed by instant formulae (I) and (II) which will be effective in releasing parent compound to its target following their in vivo administration.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-25 and 41-55 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 1-25 and 41-55, the term ---prodrug--- is indefinite since specific prodrugs and a method of preparing them are not defined.

In claims 41-44, the term ---condition mediated by a progesterone receptor --- is indefinite since specific conditions are not defined and furthermore, it is not clear whether these conditions are mediated by either hyperactivity or hypoactivity of progesterone receptor.

In claims 45 and 48, the term ---modulating---is indefinite since it is not clear whether it is directed to increased or decreased fertility or activity of progesterone receptor.

In claims 50-53, it is not clear how 50% activation of progesterone receptor is being assessed at different blood plasma concentrations of a compound?

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In claim 54, the type of cancer to be treated is not defined.

In claim 55, it is not clear whether this is directed to in vitro or in vivo method and furthermore, the steps for testing the contacted cell to determine the presence of progesterone receptor are missing. Also, it is not clear what is being used to label the compounds?

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

9. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148

USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

10. Claims 1-25 and 41-55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jones (U.S. Patent 5,696,127, cited on applicants form 1449).

Jones discloses compounds of formulae (V) and (VII) having progesterone receptor agonist/antagonist activity for treating various disease conditions (see col. 8, lines 35-65). The most closely related compounds (see examples 110, 112-115 in columns

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131-132 and examples 129, 130 in column 135) disclosed by Jones differ from the instant compounds only in having hydrogen (variable R14 in compounds of Jones) instead of fluorine at 7th position. However, the generic teachings of Jones teach that Variable R14 can also be F (see column 11, line 16) in addition to hydrogen.

Therefore, it would have been obvious to one skilled in the art to prepare the instant compounds without affecting their utility since Jones teaches this interchangeability for variable R14.

Double Patenting

11. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

12. Claims 1-25 and 41-55 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5, 7-15, 17, 19-22, 24-28, 30-33 and 35 of U.S. Patent No. 5,696,127(cited on applicants form 1449). Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant compounds of formula (I), pharmaceutical compositions

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containing these compounds and methods of using these compounds are encompassed by compounds of formula (V) of the cited patent when R12 and R14 both represent F.

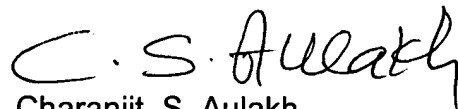
13. Claims 1-25 and 41-55 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-27 of U.S. Patent No. 5,693,646 (cited on applicants form 1449). Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant compounds of formula (II), pharmaceutical compositions containing these compounds and methods of using these compounds are encompassed by compounds of formula (VII) of the cited patent when R12 and R14 both represent F.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charanjit S. Aulakh whose telephone number is (571)272-0678. The examiner can normally be reached on Monday through Friday, 8:30 A.M. to 5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on (571)272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

A handwritten signature in black ink, appearing to read "C. S. Aulakh". The signature is fluid and cursive, with the first letters of each name being capitalized and prominent.

Charanjit S. Aulakh
Primary Examiner
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